## PROTOCOL SUMMARY:

**Protocol number: Title** VCL-1005-208: A Phase II Study of High-Dose Allovectin-7® in Patients with Advanced Metastatic Melanoma

**Tumor Type and Stage:** Stage III or IV melanoma (visceral disease limited to lung only)

**Key Inclusion Criteria:**

- Recurrent or unresponsive disease after prior standard therapy or refusal of prior therapy
- ECOG performance status of 0 or 1
- Normal serum LDH
- No prior therapy with Allovectin-7®
- At least one injectable lesion (cutaneous or nodal) $\geq 1$ cm$^2$ and $\leq 25$ cm$^2$
- No lesion $> 100$ cm$^2$

**Study Phase and Type:** Phase II, open label, multi-center

**Number of Patients:** 68 - 80 (9-24 in dose escalation stage, total of 62 evaluable patients required)

**Study Design:** An initial *dose escalation stage* will identify a safe dose Allovectin-7® given weekly for 6 weeks. Cohorts will initially consist of three patients with no intra-patient dose escalation. Subsequent cohorts will expand to 6 patients in the event that any patient experiences dose limiting toxicity.

After completing the dose escalation stage, patients will be divided into 2 groups (1 injectable lesion versus 2 or more injectable lesions) for the *efficacy stage*. Patients with 1 injectable lesion will receive Allovectin-7® weekly for 6 weeks. Patients with 2 or more injectable lesions will be randomized to injection of a single lesion or to treatment of all injectable lesions (up to 5 lesions) weekly for 6 weeks.

Stable or responding patients may receive additional treatment cycles starting at week 10 for up to a total of 4 cycles of treatment. Patients with non-clinically significant disease progression at week 10 may, at the discretion of their treating oncologist, receive a second 6-week cycle of Allovectin-7®. However, such patients must demonstrate stable or responding disease following the second cycle of therapy to receive a third and/or fourth cycle of treatment.

**Study Endpoints:** Primary objective:

- Estimate the systemic response rate to high-dose, intratumoral Allovectin-7®

Secondary objectives:

- Estimate time to progression
- Estimate duration of response
- Evaluate the toxicity of high-dose Allovectin-7®
- Evaluate the development of a cellular immune response following therapy
- Evaluate the efficiency of expression of HLA-B7
- Explore the benefit of injecting multiple lesions
- Explore the relationship between patient haplotype and response